Docket #: S17-067

Methods and compositions for the treatment of ALS/FTD and related neurodegenerative diseases

Neurodegenerative diseases amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) have been characterized by the expansion of the GGGGCC hexanucleotide repeat within the non-coding region of the human chromosome 9 open reading frame 72 (C9ORF72) gene. However, the impact of this genetic footprint on disease pathology is poorly understood, limiting the development of therapeutics against the diseases.

Researchers at Stanford's Lu laboratory have profiled the molecular impact of the peptides produced by the expansion of C9ORF72. The newly implicated pathways include molecular targets with known pharmacological agents that can re-purposed and optimized, such as the antiporter nigericin or AKT activator SC79, where the inventors have demonstrated that pharmacological targeting can rescue ALS phenotypes in various animal models. Other pathways implicated by the inventors for their role in ALS and FTD, including AKT, Notch, and numerous mitochondrial proteins, can be manipulated by genetic modifiers or small molecules.

Applications

- Treatment of neurodegenerative disorders ALS and FTD
- Possible extensions in Parkinson's disease, Huntington's disease, spinocerebellar ataxia type 8 (SCA8), myotonic dystrophy type 1 (DM1), and fragile X tremor ataxia syndrome (FXTAS)

Advantages

- Potential to re-purpose existing compounds that target molecular pathways implicated in ALS and FTD
- Opportunity for the first disease-modifying therapy in indications with limited treatment options
- Offers small molecule alternatives and potential oral delivery as an alternative to the antisense oligos currently in ALS R&D pipelines

Publications

- S. Li et al Altered MICOS morphology and mitochondrial Ion Homeostasis Contribute to Poly(GR) Toxicity Associated with C9-ALS/FTD *Cell Rep* 2020 Aug 4.

Patents

- Published Application: 20220389067

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